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Clinical and Demographic Predictors of Outcomes in Recent Onset Dilated Cardiomyopathy

Results of the IMAC (Intervention in Myocarditis and Acute Cardiomyopathy)-2 Study

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Objectives We sought to determine clinical and demographic predictors of recovery of left ventricular function for subjects with recent onset cardiomyopathy (ROCM).

Background Although ROCM is a frequent reason for consultation and transplantation referral, its prognosis and natural history on contemporary therapy are unknown.

Methods In the multicenter IMAC (Intervention in Myocarditis and Acute Cardiomyopathy)-2 study, subjects with a left ventricular ejection fraction (LVEF) of ≤0.40, fewer than 6 months of symptom duration, and an evaluation consistent with idiopathic dilated cardiomyopathy or myocarditis were enrolled. LVEF was reassessed at 6 months, and subjects were followed up for 4 years. LVEF and event-free survival were compared by race, sex, and clinical phenotype.

Results The cohort of 373 persons was 38% female and 21% black, with a mean age of 45 ± 14 years. At entry, 91% were receiving angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and 82% were receiving beta-blockers, which increased to 92% and 94% at 6 months. LVEF was 0.24 ± 0.08 at entry and 0.40 ± 0.12 at 6 months (mean increase: 17 ± 13 ejection fraction units). Transplant-free survival at 1, 2, and 4 years was 94%, 92%, and 88%, respectively; survival free of heart failure hospitalization was 88%, 82%, and 78%, respectively. In analyses adjusted for sex, baseline LVEF, and blood pressure, LVEF at 6 months was significantly lower in blacks than in nonblacks ($p = 0.02$). Left ventricular end-diastolic diameter at presentation was the strongest predictor of LVEF at 6 months ($p < 0.0001$).

Conclusions Outcomes in ROCM are favorable but differ by race. Left ventricular end-diastolic diameter by transthoracic echo at presentation was most predictive of subsequent myocardial recovery. (Genetic Modulation of Left Ventricular Recovery in Recent Onset Cardiomyopathy; NCT00575211) (J Am Coll Cardiol 2011;58:1112–8) © 2011 by the American College of Cardiology Foundation

Idiopathic dilated cardiomyopathy remains an important cause of systolic heart failure and the most common cause of heart failure in young people referred for cardiac transplantation (1). With a prevalence estimated at 36 cases per 100,000 (2), this disorder affects well over 100,000 people in the United States alone. An inflammatory pathogenesis is suspected (3); however, endomyocardial biopsy demonstrates inflammation in only a small subset of patients (4). Treatment with immune modulatory therapy has not proven effective for recent onset cardiomyopathy (ROCM) (5,6), nor in the subset with cellular myocarditis (7).

Myocardial recovery occurs in one-third of subjects with ROCM, defined as fewer than 6 months of cardiac symptoms. Most previous reports (8) in ROCM predate the widespread use of beta-blockers, and the prognosis and natural

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history on contemporary therapy mostly are unknown. We initiated a multicenter investigation of myocardial recovery in subjects with ROCM to determine the demographic and clinical predictors of subsequent left ventricular recovery.

Methods

The IMAC (Intervention in Myocarditis and Acute Cardiomyopathy)-2 study was a prospective, multicenter investigation of myocardial recovery in subjects with recent onset (i.e., acute) nonischemic dilated cardiomyopathy and myocarditis that enrolled subjects at 16 centers (Online Appendix) from May 2002 through December 2008. All subjects had a left ventricular ejection fraction (LVEF) of 0.40 or less by echocardiography and symptoms of <6 months in duration. Informed consent was obtained from all subjects, and the protocol was approved by the institutional review boards of all participating centers.

Demographic information included self-designated race (white, black, Asian, or other). Subjects underwent angiography or noninvasive screening to exclude coronary artery disease and transthoracic echocardiography to rule out valvular disease. Patients with significant diabetes (requiring therapy with insulin or an oral agent for more than 1 year), uncontrolled hypertension (diastolic blood pressure more than 95 mm Hg or systolic blood pressure more than 160 mm Hg), suspected alcoholism, tachycardia-induced cardiomyopathy, uncorrected thyroid disease, or systemic disorders with associated cardiomyopathy, such as lupus erythematosus, hemochromatosis, or sarcoidosis, were excluded. Right ventricular endomyocardial biopsy was not required based on current practice guidelines (9).

LVEF was assessed by transthoracic echocardiography at entry and at 6 months, and patients were followed up for up to 48 months. All deaths and hospitalizations were adjudicated by an independent events committee. The primary outcome was change in LVEF from baseline to 6 months. Secondary outcomes included transplant-free survival and hospitalization-free survival.

Echocardiography. Echocardiographic studies were reviewed in a blinded fashion by a core laboratory at the University of Pittsburgh. Digital routine grayscale 2-dimensional cine loops were obtained at frame rates of 40 to 90 Hz (mean: 60 ± 15 Hz) from standard apical 4-chamber, 2-chamber, and long-axis views. The left ventricle (LV) volume and LVEF were assessed by biplane Simpson's rule using manual tracing of digital images. Left ventricular end-diastolic diameter (LVEDD) was assessed in the parasternal long-axis view.

Statistical analysis. Demographic and clinical characteristics were compared by sex and race (black vs. nonblack), with continuous variables compared by Student *t* tests and categorical variables compared by use of the Fisher exact test. For the analysis of LVEDD and myocardial recovery, comparisons first were made based on a simple arbitrary division chosen for clinical usefulness. Subjects were grouped based on LVEDD at presentation into those with minimal dilation, <6.0 cm, moderate dilation, 6.0 to 7.0 cm, and severe dilation, >7.0 cm. Analysis then was repeated using sex-specific tertiles. This included use of general linear models and a 1-degree of freedom linear contrast (coded −1, 0, 1) to evaluate whether the extent of myocardial recovery varied monotonically with respect to tertiles of LVEDD. In multivariate analysis, multiple linear regression was used to identify independent predictors of change in LVEF at 6 months (i.e., verified as approximately normally distributed). Covariates were selected by use for stepwise selection (forward) with an entry and retainment p value of 0.05, and age was included regardless of statistical significance. Before assessment of main effects, the interaction between race and both systolic and diastolic blood pressure was examined.

Abbreviations and Acronyms

LV = left ventricle/ventricular

LVEDD = left ventricular end-diastolic diameter

LVEF = left ventricular ejection fraction

NYHA = New York Heart Association

ROCM = recent onset cardiomyopathy

Survival analysis methods were based on 3 endpoints: death, death or transplantation, and a composite endpoint that included death, transplantation, and heart failure hospitalization. The Kaplan-Meier method was used to estimate event-free survival and curves compared by the log-rank test. In multivariate analysis, Cox regression was used to estimate adjusted hazard ratios for the endpoints death/transplantation and the composite endpoint. Stepwise selection (forward) was used to identify independent predictors of these endpoints, with race (black, nonblack) and diastolic blood pressure (more or less than the median of 70 mm Hg) combined into 4 groups to yield estimates of interaction effects (because of the significant interaction). The proportional hazards assumption of invariant relative risk was tested formally and was found to be upheld for all variables and endpoints assessed with 2 minor exceptions. For risk of death/transplantation, the hazard ratio associated with New York Heart Association (NYHA) functional class IV was more pronounced in the first year of follow-up; for risk of the composite endpoint, there was an indication that risk increased in a nonproportional manner over follow-up among black patients with diastolic blood pressure of <70 mg/dl at baseline. For these 2 exceptions, separate risk estimates were reported for early follow-up.

Results

The cohort of 373 subjects was 21% (n = 80) black and 38% (n = 143) women, including 39 (10%) with peripartum cardiomyopathy. The mean age was 45 ± 14 years, LVEF was 0.24 ± 0.08, symptom duration was 2.2 ± 1.7 months, and percent NYHA functional class I, II, III, and IV was 18%, 46%, 29%, and 7%, respectively. Forty-four (12%) subjects underwent an endomyocardial biopsy that revealed

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inflammation in 15 (4.0%) subjects and myocarditis in only 10 (2.6%) subjects.

Therapy at entry included an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker in 91%, beta-blocker in 82%, aldosterone receptor antagonist in 27%, and loop diuretic in 67% (predominantly furosemide in 96%, mean daily dose: 57 ± 43 mg). At entry, 28 (7.5%) subjects had an implantable cardiac defibrillator (implantable cardioverter-defibrillator), 28 (7.5%) were receiving intravenous inotropic therapy, 3 (0.8%) had an intra-aortic balloon pump, and 6 (1.6%) had an LV assist device.

At 6 months, 92% were receiving an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, 94% were receiving beta-blockers, 20% had an implantable cardioverter-defibrillator, and the percent of subjects with NYHA functional class I, II, III, and IV was 45%, 44%, 9%, and 1%, respectively. The mean LVEF was 0.40 ± 0.12 (n = 327), with an increase of 17 ± 13 ejection fraction units (n = 312). Overall, 70% demonstrated an increase at 6 months of at least 10 ejection fraction units, and 39% demonstrated an increase of 20 U or more. Forty percent had an LVEF of 0.45 or more at 6 months, and for 25%, the LVEF had normalized (0.50 or more). The percent of subjects whose LVEF normalized differed by sex (men: 20%, women: 34%, p = 0.004) with a trend toward less recovery in blacks (blacks: 18%, nonblacks: 27%, p = 0.14). Combining the demographic factors, an LVEF of 0.50 or more at 6 months was most likely in white women (38%), least likely in black men (15%), and intermediate in white men (21%) and black women (20%).

The mean follow-up was 2.2 ± 1.4 years. During follow-up, there were 14 deaths (4%), 17 transplantations (5%), 45 hospitalizations for heart failure (12%) in the absence of death or transplantation, and 62 (17%) hospitalizations for heart failure in aggregate with a survival at 1, 2, and 4 years of 98%, 96%, and 94%, respectively, transplant-free survival of 94%, 92%, and 88%, respectively (Fig. 1A), and survival free of the composite endpoint of 88%, 82%, and 78%, respectively. Prognosis was dependent on functional class at presentation, with percent transplant-free survival at 1 year for NYHA functional class I, II, III, and IV of 100%, 98%, 87%, and 75% (p < 0.0001) (Fig. 1B). A similar finding was evident based on hemodynamic support, because more subjects receiving intravenous inotropic therapy at entry died (18% vs. 3%) or underwent transplantation (18% vs. 4%) during follow-up (p < 0.001).

Sex and outcomes. Myocardial recovery was more evident in women, with a similar baseline LVEF of 0.24 ± 0.08 in women versus 0.23 ± 0.08 in men (p = 0.09) and a larger LVEF at 6 months of 0.43 ± 0.12 in women versus 0.39 ± 0.12 in men (p = 0.004) (Table 1). Transplant-free survival was significantly better in women (1-, 2-, and 4-year percent transplant-free survival for women: 96%, 96%, and 96%, for men: 93%, 90%, and 84%, p = 0.03), driven by a marked difference in survival (p = 0.003).

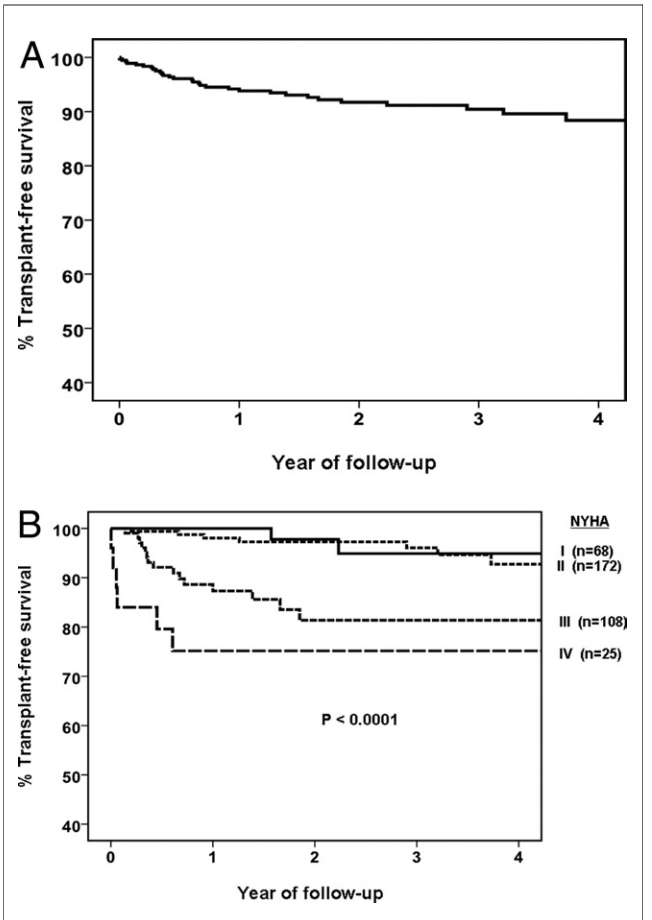

Figure 1 Transplant-Free Survival

Graphs showing transplant-free survival in **(A)** the overall cohort (n = 373) and **(B)** stratified by New York Heart Association (NYHA) functional class (for classes I, II, III, and IV, n = 68, 172, 108, and 25, respectively). Higher functional class is associated with poorer event-free survival (p < 0.0001).

Race and outcomes. The cohort included 80 black subjects (21%) and 293 nonblack subjects (79%: 272 white, 9 Asian, and 12 other). Medical therapy with angiotensin-converting enzyme inhibitors and beta-blockers was comparable (Table 1). Hydralazine and nitrates were received by 9% of blacks and 2% of nonblacks (p = 0.005). The black cohort was younger (range: 42 ± 12 years, nonblack: 46 ± 14 years, p = 0.02), with higher diastolic blood pressure at entry (mean diastolic for blacks: 74 ± 13 mm Hg, mean diastolic for nonblacks: 70 ± 12 mm Hg, p = 0.005, and systolic for blacks: 115 ± 19 mm Hg, systolic for nonblacks: 111 ± 19 mm Hg, p = 0.10) and heart rate (blacks: 87 ± 17 beats/min, nonblacks: 82 ± 17 beats/min, p = 0.02). Aldosterone receptor antagonist use was greater in blacks (p = 0.007) and was driven by use in subjects with advanced heart failure (for NYHA functional class III and IV: 53% of blacks on therapy vs. 28% of nonblacks, p = 0.01).

LVEF was similar at baseline (blacks: 0.23 ± 0.08, nonblacks: 0.24 ± 0.08, p = 0.33), but was lower in blacks at 6 months (blacks: 0.37 ± 0.13, nonblacks: 0.41 ± 0.12,

Table 1 Demographic and Clinical Characteristics by Sex and Race

By Sex	All (n = 373)	Men (n = 230)	Women (n = 143)	p Value
Age (yrs)	45 ± 14	46 ± 14	43 ± 14	0.01
Black	21.5	19.1	25.2	0.19
NYHA functional class I/II/III/IV	18/46/29/7	20/45/27/7	15/48/31/6	0.53
LVEF baseline	0.24 ± 0.08	0.23 ± 0.08	0.24 ± 0.08	0.09
LVEF at 6 months	0.40 ± 0.12	0.39 ± 0.12	0.43 ± 0.12	0.004
BP systolic	112 ± 19	113 ± 20	111 ± 17	0.27
BP diastolic	71 ± 13	71 ± 13	71 ± 13	0.97
Heart rate	83 ± 17	83 ± 17	83 ± 16	0.86
Therapy at entry				
ACE inhibitor	82.3	84.3	79.0	0.21
Aldosterone receptor antagonist	27.4	29.1	24.5	0.34
Beta-blocker	82.0	80.9	83.9	0.49

By Race	Nonblack (n = 293)	Black (n = 80)	
Age (yrs)	46 ± 14	42 ± 12	0.02
Female	36.5	40.0	0.19
NYHA functional class I/II/III/IV	20/46/26/8	11/46/40/3	0.02
LVEF baseline	0.24 ± 0.08	0.23 ± 0.08	0.33
LVEF at 6 months	0.41 ± 0.12	0.37 ± 0.13	0.007
BP systolic	111 ± 19	115 ± 19	0.10
BP diastolic	70 ± 12	74 ± 13	0.005
Heart rate	82 ± 17	87 ± 17	0.02
Therapy at entry			
ACE inhibitor	82.9	80.0	0.51
Aldosterone receptor antagonist	23.9	40.0	0.007
Beta-blocker	80.5	87.5	0.19

Values are mean ± SD or %.
ACE = angiotensin converting enzyme; BP = blood pressure; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association.

p = 0.007). Clinical outcomes were worse in blacks for transplant-free survival (1, 2, and 4 years, black: 90%, 85%, and 72%, nonblacks: 95%, 93%, and 92%, p = 0.01) (Fig. 2A) and survival free of the composite endpoint (1, 2, and 4 years, black: 83%, 69%, and 50%, nonblacks: 90%, 86%, 83%, p = 0.001) (Fig. 2B). Similar results were observed when the nonblack group was restricted to the 272 (93.5%) of 293 subjects with self-designated race classified as white (data not shown).

LVEDD and myocardial recovery. Overall the mean LVEDD was 6.3 ± 1.0 cm. When dividing subjects into those with minimal dilation (group 1: LVEDD < 6.0 cm, n = 125), moderate dilation (group 2: 6.0 to 7.0 cm, n = 139), or severe dilation (group 3: > 7.0 cm, n = 67), LVEF at baseline (groups 1, 2, and 3: 0.27 ± 0.08, 0.23 ± 0.08, and 0.20 ± 0.07, respectively, p < 0.0001), LVEF at 6 months (groups 1, 2, and 3: 0.45 ± 0.11, 0.40 ± 0.11, and 0.32 ± 0.12, respectively, p < 0.0001), and change in LVEF (groups 1, 2, and 3: 0.19 ± 0.12, 0.17 ± 0.13, and 0.13 ± 0.13, respectively, p = 0.005) were greatest for group 1, intermediate for group 2, and lowest for group 3 (Fig. 3A). This analysis was repeated using sex-specific tertiles, and a similar association of smaller LVEDD with greater recovery was evident for both women (Fig. 3B) and men (Fig. 3C).

Multivariate analyses. Independent predictors of LVEF at 6 months of follow-up are provided in rank order in Table 2. A smaller LVEDD at baseline was associated with higher LVEF at 6 months (p < 0.0001), independent of sex (p = 0.75). Higher systolic blood pressure at baseline also was associated with LVEF at 6 months (p = 0.001), whereas black race (p = 0.02) and higher NYHA functional class (p = 0.04) were associated with lower LVEF at 6 months. These associations occurred independent of baseline LVEF, which was included as a covariate and was not associated with LVEF at 6 months (p = 0.32). In total, the 7 variables included in the multiple linear regression model explained 25% of the variation in LVEF at 6 months. The interaction between race and systolic blood pressure (p = 0.96), as well as diastolic pressure (p = 0.63), was not statistically significant (data not shown), indicating that the effect of race was independent of baseline blood pressure. Similar results were observed when the outcome (dependent) variable was absolute change in LVEF between baseline and 6 months (Table 2).

Predictors of death/transplantation and the composite endpoint are provided in Table 3. As seen, NYHA functional class IV (adjusted hazard ratio: 9.41) and black race (adjusted hazard ratio: 2.78) were associated with a significantly higher risk of death/transplantation over

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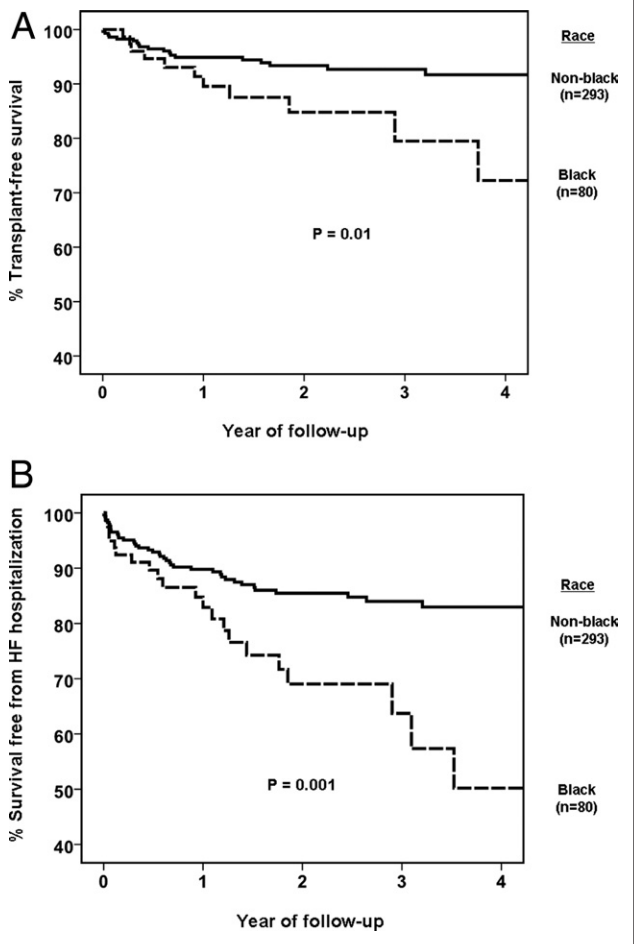

Figure 2 Clinical Outcomes by Race

(A) Graph showing transplant-free survival (black [n = 80] vs. nonblack [n = 293]). Event-free survival is worse in black patients (p = 0.01). **(B)** Graph showing survival free of heart failure hospitalization (black [n = 80] vs. nonblack [n = 293]). Event-free survival is worse in black patients (p = 0.001).

4 years of follow-up. In contrast, female sex (adjusted hazard ratio: 0.34) was associated with a significantly lower risk of death/transplantation. Compared with white patients with diastolic blood pressure of 70 mg/dl or more at baseline, black patients with diastolic blood pressure of more than 70 mg/dl has an estimated 5-fold higher risk of death/transplantation. Results generally were consistent for the broader outcome of risk of the composite endpoint; however, black patients were at higher risk than white patients regardless of baseline diastolic blood pressure.

Discussion

Recent onset dilated cardiomyopathy remains a challenging diagnosis for patients and clinicians alike and frequently results in referral to tertiary centers. The current study demonstrates that there is substantial improvement in LVEF evident for most subjects over the first 6 months. Despite concerns, the short-term the prognosis is favorable, with a transplant-free survival of 88% at 4 years.

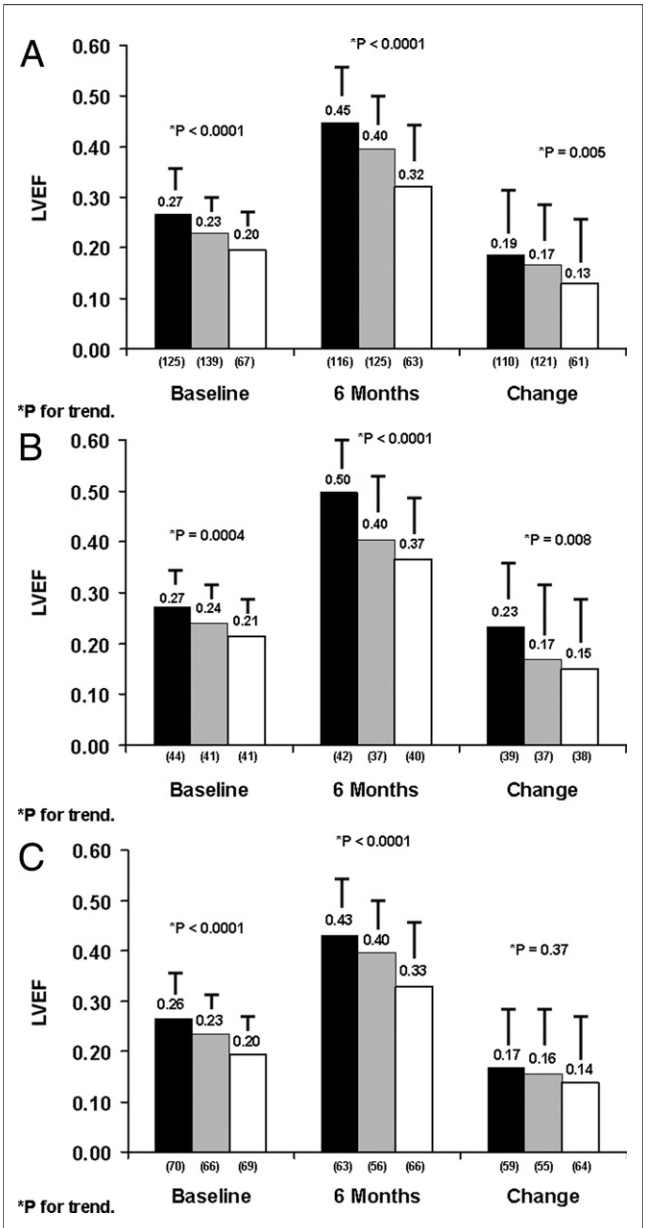

Figure 3 Myocardial Recovery by LVEDD

(A) Bar graph showing myocardial recovery by left ventricular end-diastolic diameter (LVEDD) for the entire cohort: **solid bars** = LVEDD <6.0 cm; **shaded bars** = LVEDD 6.0 to 7.0 cm; **open bars** = LVEDD >7.0 cm. Left ventricular ejection fraction (LVEF) at entry (p < 0.0001), LVEF at 6 months (p < 0.0001), and left ventricle change (p = 0.005) all were significantly greater with smaller LVEDD. **(B)** Bar graph showing myocardial recovery by LVEDD for women: **solid bars** = LVEDD ≤5.5 cm; **shaded bars** = LVEDD 5.6 to 6.1 cm; **open bars** = LVEDD >6.1 cm. The LVEF at entry (p = 0.0004), LVEF at 6 months (p < 0.0001), and left ventricle LV change (p = 0.008). **(C)** Bar graph showing myocardial recovery by LVEDD for men: **solid bars** = LVEDD ≤6.1 cm; **shaded bars** = LVEDD 6.2 to 6.9 cm; **open bars** = LVEDD >6.9 cm. The LVEF at entry (p < 0.0001), LVEF at 6 months (p < 0.0001), and left ventricle LV change (p = 0.37). The **label on each bar** represents mean LVEF for the subset. **Error bar** represents standard deviation.

Table 2 Predictors of LVEF and Change in LVEF at 6 Months (n = 292)

Variable	t Value	Standardized Coefficient	Semipartial^2 Correlation	p Value
LVEF				
LVEDD	−6.98	−0.41	0.13	<0.0001
Systolic BP	3.30	0.18	0.03	0.001
Black race	−2.39	−0.12	0.01	0.02
NYHA functional class	−2.10	−0.11	0.01	0.04
Age	−1.25	−0.07	0.004	0.21
Baseline LVEF	1.00	0.06	0.003	0.32
Female	0.32	0.02	0.0003	0.75
Adjusted R^2 = 0.25				
Change in LVEF				
Baseline LVEF	−10.91	−0.59	0.28	<0.0001
LVEDD	−6.98	−0.39	0.11	<0.0001
Systolic BP	3.30	0.17	0.03	0.001
Black race	−2.39	−0.12	0.01	0.02
NYHA functional class	−2.10	−0.11	0.01	0.04
Age	−1.25	−0.06	0.004	0.21
Female	0.32	0.02	0.0002	0.75
Adjusted R^2 = 0.32				

LVEDD = left ventricular end-diastolic diameter; other abbreviations as in Table 1.

The dynamic nature of ROCM long has been recognized, and the percent of patients normalizing their ejection fraction (25%) in the current series does not differ significantly from that of previous investigations (4,6,8). However, the percentage of subjects experiencing at least moderate recovery of LV function, that is, 10 ejection fraction units or more, has improved dramatically from one third in an older series (4,8) to one-half in the previous Intervention in Myocarditis and Acute Cardiomyopathy trial (6), to nearly 70% of subjects in the current cohort. Given the impact of beta-blockers in chronic nonischemic cardiomyopathy (10,11), the widespread improvements in LVEF in the current investigation can be attributed in part to their extensive use in this cohort.

An inflammatory pathogenesis is postulated for subjects with so-called reversible cardiomyopathy, in which the recovery ensues when the inflammatory event resolves (12). Indeed, for subjects with histological confirmation of lymphocytic myocarditis, the mean LVEF at 6 months was 0.49 ± 0.08. Although myocardial inflammation may be a potential marker of reversibility, additional methodologies, including cardiac magnetic resonance and novel peripheral biomarkers, may be more effective than endomyocardial biopsy at delineating reversible inflammatory myocarditis (13).

Women had better outcomes than men in terms of LVEF at 6 months and transplant-free survival. A similar trend toward better recovery in women was seen in the first IMAC trial. Analysis of myocardial gene expression in that trial demonstrated that activation of apoptotic pathways was associated inversely with recovery (14) and that this activation was less evident in women. The recovery of LVEF in the current study is consistent with investigations in chronic heart failure in which women generally have better outcomes than their male counterparts (15).

Self-identified black subjects demonstrated less recovery and markedly worse transplant-free survival. The impact of race in recent onset cardiomyopathy again parallels findings in chronic heart failure (16). It long has been recognized that hypertension is more prevalent in blacks as a cause of heart failure. Although multivariate analysis did not suggest that racial differences by race could be attributed to blood pressure, this was based a single baseline measurement, and does not address the potential impact of chronic hypertension. Whether outcomes by race reflect a differential genomic response to therapy or other socioeconomic variables will require further analysis.

Table 3 Predictors of Death/Transplantation and HF Hospitalization

	Death/Transplantation (n = 373)			HF Hospitalization (n = 373)		
Predictor	Adjusted HR	95% CI	p Value	Adjusted HR	95% CI	p Value
NYHA functional class						
II (vs. I)	1.19	0.25–5.71	0.83	1.04	0.43–2.48	0.94
III (vs. I)	4.16	0.93–18.63	0.06	1.52	0.62–3.74	0.36
IV (vs. I)	9.41*	1.83–48.32	0.007†	3.50	1.22–10.02	0.02‡
Age (per 10 yrs)	0.77	0.59–1.01	0.06	0.85	0.70–1.04	0.12
Female	0.34	0.14–0.83	0.02	0.57	0.32–0.99	0.05
Heart rate (per 10 beats)	—	—	—	1.21	1.03–1.43	0.02
Race and diastolic BP§						
White, DBP <70 mg/dl	2.07	0.79–5.43	0.14	1.85	0.97–3.53	0.06
Black, DBP <70 mg/dl	2.11	0.41–10.84	0.38	3.65	1.51–8.82	0.004‖
Black, DBP ≥70 mg/dl	4.97	1.69–14.60	0.004	2.94	1.37–6.32	0.006

*The estimated adjusted hazard ratio in the first 2 years of follow-up was 18.2 (95% CI: 2.13 to 155.5), indicating higher risk early in follow-up compared with the average risk estimate of 9.41 estimated for the entire follow-up period. †The p value for NYHA functional class as an ordered variable was < 0.0001. ‡The p value for NYHA functional class as an ordered variable was 0.01. §The referent group is white, DBP ≥70 mg/dl; the white classification includes all races self-reported other than black. ‖The estimated adjusted hazard ratio in the first years of follow-up was 1.76 (95% CI: 0.47 to 6.65), indicating lower risk early in follow-up compared with the average risk estimate of 3.65 estimated for the entire follow-up period.

CI = confidence interval; DBP = diastolic blood pressure; HF = heart failure; HR = hazard ratio; other abbreviation as in Tables 1 and 2.

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In terms of the initial assessment, LVEDD was most predictive, because less LV enlargement at presentation predicted a greater LVEF at 6 months. In a recent analysis of subjects supported with a left ventricular assist device, myocardial recovery occurred in 12% of subjects overall, but 33% of subjects with LVEDD <6.0 cm (17). Smaller LV size likely is a marker of a more reversible cardiac pathological condition and LVEDD remains a simple standard echo measure routinely reported that can provide immediate clinical guidance in predicting recovery potential.

Study limitation. A limitation of this study is the overall low number of so-called hard events in the analysis (i.e., death/transplantation). The net consequence of this is relatively imprecise estimates of long-term risk of death/transplantation and heart failure hospitalization. This limitation should be kept in mind when interpreting the relative predictive value of individual variables.

Conclusions

Contemporary heart failure therapy has changed the natural history of recent onset cardiomyopathy from a rapidly progressive disorder to a more manageable condition with an overall favorable prognosis. Indeed, most subjects have significant improvements in LVEF during the first 6 months. Recognition of this recovery potential is essential, and advanced therapies such as cardiac transplantation should not be undertaken until clinicians observe the early clinical course to determine the degree of recovery. Although these results are encouraging, outcomes remain heterogeneous; in particular, recovery and survival were poorer in black subjects. The basis for these apparent racial differences is unknown, and additional investigation is required to delineate the biologic and genomic determinants of myocardial recovery in ROCM.

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Key Words: cardiomyopathy ■ echocardiography ■ myocardial function ■ outcomes ■ recovery.

APPENDIX

For a full list of the IMAC Investigators, please see the online version of this article.